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Asymmetric hydrogenation by ruthenium cluster hydrides containing atropoisomeric diphosphine ligands

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Abstract

Ruthenium clusters containing atropoisomeric diphosphines, namely $[Ru_4(\mu\text{-}H)_4(CO)_{10}\{(S)\text{-}(-)\text{-BINAP}\}]$, where BINAP is 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl and $[Ru_4(\mu\text{-}H)_4(CO)_{10}\{(S)\text{-}(-)\text{-MOBIPH}\}]$, where MOBIPH is 2,2′-bis(diphenylphosphino)-6,6′-dimethoxy-1,1′-diphenyl, have been used as catalysts in the asymmetric hydrogenation of some prochiral substrates containing C=C or C=O double bonds. With the BINAP derivative optical purities up to 30% were achieved.

Keywords: Asymmetric synthesis; Hydrogenation; Ruthenium; Cluster; Atropoisomeric diphosphine

1. Introduction

Several mononuclear Ru complexes containing the atropoisomeric diphosphine ligand (*S*)-(−)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP) have been successfully used as catalysts for asymmetric reactions [1–6].

Taking into account the excellent results obtained with the BINAP ligand, other atropoisomeric diphosphines have been tested in catalysis [7]. Among these ligands, (*S*)-(−)-2,2′-bis(diphenylphosphino)-6,6′-dimethoxy-1,1′-diphenyl (MOBIPH) has also been employed in asymmetric hydrogenations [8].

To the best of our knowledge no polynuclear ruthenium species containing this kind of diphosphines has been yet tested in catalysis even though clusters containing the bidentate ligand (4*R*,5*R*)-(−)-4,5-bis[(diphenylphosphino)methyl]-2,2′-dimethyl-1,3-dioxolane (DIOP) are known to give good results in asymmetric reactions such as hydrogenation [9], isomerization [10], and hydroformylation [11]. Therefore we have thought it interesting to synthesise new ruthenium clusters containing BINAP or the analogous MOBIPH as ligand and to test their catalytic activity.

In this paper we report the catalytic data obtained in the hydrogenation of some prochiral substrates containing C=C or C=O double bonds carried out in the presence of tetraruthenium cluster complexes $[Ru_4(\mu\text{-}H)_4(CO)_{10}\{(S)\text{-}(-)\text{-BINAP}\}]$ **1** or $[Ru_4(\mu\text{-}H)_4(CO)_{10}\{(S)\text{-}(-)\text{-MOBIPH}\}]$ **2**. The synthesis and structural characterisation of these complexes has already been published [12].

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2. Results and discussion

The structure of the catalysts **1** and **2**, established by X-ray crystallographic studies [12], is schematised in Fig. 1 together with that of the two atropoisomeric diphosphines used in this work. In both clusters the ligand chelates to the apical ruthenium atom and the four hydrides bridge between adjacent ruthenium atoms (Fig. 1).

The substrates were chosen among different classes of products such as simple olefins, ketones, α,β-unsaturated carboxylic acids or esters and unsaturated dicarboxylic acids to highlight some important aspects of the interactions existing between the cluster used as catalytic precursor and the substrate such as concurrent isomerizations, steric and electronic influences, coordination modes with different functional groups etc.

In Table 1 are reported the data obtained in the hydrogenation of various prochiral substrates in the presence of cluster **1**. This catalyst results to be very active in the hydrogenation of simple olefins: thus 2-phenyl-3,3-dimethylbut-1-ene is the one most rapidly reduced, even if the o.p. is not very high (11.1%).

The best enantioface discrimination is achieved in the hydrogenation of (*E*)-2-methyl-2-butenoic acid (tiglic acid) (Table 1). In this case good conversions are obtained in reasonable reaction times. The hydrogenation of the corresponding ethyl ester (ethyl tiglate) gives ethyl 2-methylbutanoate with significantly lower enantioselectivity and reaction rate. Therefore it appears that, as found in many other cases of catalysis with ruthenium complexes [4,13], the presence of a carboxylic group on the substrate serves to strengthen the interaction between the olefin and the catalyst. This secondary inductive effect is weak, or completely absent, in the case of the corresponding unsaturated ester [4,13].

The data reported in Table 1 show that the asymmetric hydrogenation of (*E*)-2-methyl-

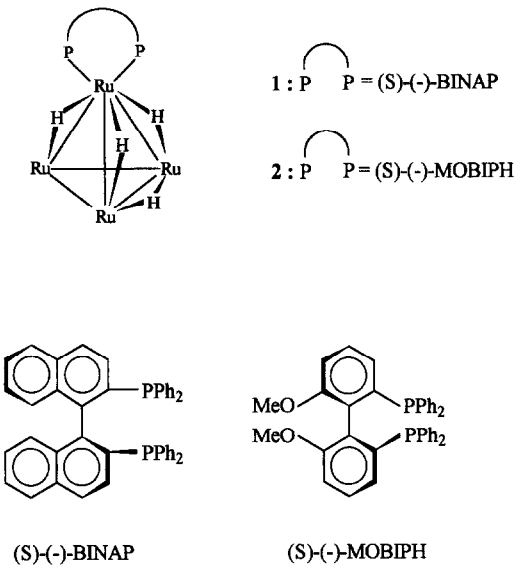

Fig. 1. Structure of catalysts **1** and **2** and of the ligands used.

Table 1
Hydrogenation of various unsaturated substrates in the presence of $[Ru_4(\mu\text{-H})_4(CO)_{10}\{(S)\text{-}(-)\text{-BINAP}\}]$

Substrate	Product	*t* (h)	Conversion (%)	Yield (%)	o.p. [a] (%)	Configuration	Solvent
(*E*)-2-methyl-2-butenoic acid	2-methylbutanoic acid	93	90.5	84.7 [b]	28.5	(*R*)	toluene/ethanol (1/1)
ethyl (*E*)-2-methyl-2-butenoate	ethyl 2-methylbutanoate	234	87.4	87.4	2.9	(*R*)	toluene/ethanol (1/1)
acetophenone	1-phenylethanol	408	49.5	49.5	1.5	(*R*)	toluene
2-phenyl-3,3-dimethylbut-1-ene	2-phenyl-3,3-dimethylbutane	64	100	100	11.1	(*R*)	toluene
(*Z*)-2-methylbutendioic acid	2-methylsuccinic acid	142	93.1	45.4 [c]	13.2	(*S*)	toluene/THF (1/1)
(*E*)-2-methylbutendioic acid	2-methylsuccinic acid	165	88.5	76.6 [d]	10.4	(*R*)	toluene/THF (1/1)
2-phenylpropenoic acid	2-phenylpropionic acid	72	86.0	86.0	6.3	(*S*)	toluene/THF (1/1)

Reaction conditions: $T = 100°C$; solvent = 20 ml; substrate = 0.038 mmol; substrate/catalyst = 2000 mol/mol; $P(H_2) = 130$ bar.
[a] Optical purity measured on samples of purified product using the corresponding $[\alpha]_{max}$ values reported in the Experimental part.
[b] 5.8% of ethyl (*E*)-2-methyl-2-butenoate is also formed.
[c] 26.5% of (*Z*)-2-methylbutendioic anhydride and 21.2% of 2-methylsuccinic anhydride are also formed.
[d] 11.9% of 2-methylsuccinic anhydride is also formed.

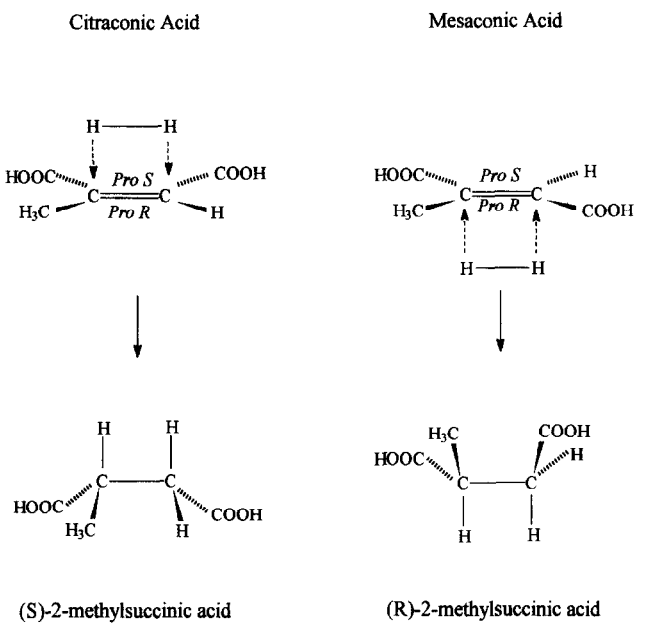

Fig. 2. Steric course of hydrogen addition to citraconic and mesaconic acids.

butendioic acid (mesaconic acid) gives (*R*)-2-methylsuccinic acid, while that of (*Z*)-2-methylbutendioic acid (citraconic acid) brings to the opposite (*S*) stereoisomer. Since a simple examination of Fig. 2 shows that the front face of both substrates under investigation is pro-*S*, the hydrogen addition must occur from the front face in the case of citraconic acid and from the rear face for mesaconic acid [14]. This is probably due to a different interaction of the metal centre with the carboxylic groups in the (*Z*) or (*E*) position [14] allowing the catalyst to distinguish between the enantiofaces of the prochiral substrates.

Catalyst **1** is fairly active in the hydrogenation of unsaturated substrates: for example, 2-phenylpropenoic acid (atropic acid) reacts in a relatively short time (72 h), even if the o.p. of the product is quite low (6.3%). In the case of acetophenone, the only tested ketone, the reaction is very slow and the o.p. close to zero.

Similar results are obtained for the hydro-

Table 2
Hydrogenation of various unsaturated substrates in the presence of $[Ru_4(\mu\text{-}H)_4(CO)_{10}\{(S)\text{-}(-)\text{-MOBIPH}\}]$

Substrate	Product	t (h)	Conversion (%)	Yield (%)	o.p. [a] (%)	Configuration	Solvent
(*E*)-2-methyl-2-butenoic acid	2-methylbutanoic acid	72	100	93.7 [b]	16.7	(*S*)	toluene/ethanol (1/1)
ethyl (*E*)-2-methyl-2-butenoate	ethyl 2-methylbutanoate	253	100	100	1.8	(*S*)	toluene/ethanol (1/1)
acetophenone	1-phenylethanol	72	45.6	45.6	0.2	(*S*)	toluene
(*Z*)-2-methylbutendioic acid	2-methylsuccinic acid	72	89.9	67.6 [c]	4.9	(*S*)	toluene/THF (1/1)
(*E*)-2-methylbutendioic acid	2-methylsuccinic acid	47	70.5	60.4 [d]	3.5	(*R*)	toluene/THF (1/1)
2-phenylpropenoic acid	2-phenylpropionic acid	72	57.0	57.0	4.2	(*S*)	toluene/THF (1/1)

Reaction conditions: $T = 100°C$; solvent = 20 ml; substrate = 0.038 mmol; substrate/catalyst = 2000 mol/mol; $P(H_2) = 130$ bar.

[a] Optical purity measured on samples of purified product using the corresponding $[\alpha]_{max}$ values reported in the Experimental part.

[b] 6.3% of ethyl (*E*)-2-methyl-2-butenoate is also formed.

[c] 7.9% of (*Z*)-2-methylbutendioic anhydride and 14.4% 2-methylsuccinic anhydride are also formed.

[d] 10.1% of 2-methylsuccinic anhydride is also formed.

Table 3
Influence of temperature on the hydrogenation of tiglic acid in the presence of $[Ru_4(\mu\text{-}H)_4(CO)_{10}\{(S)\text{-}(-)\text{-BINAP}\}]$

T (°C)	t (h)	Conversion (%)	Yield [a] (%)	o.p. [b] (%)	Configuration
120	43	89.2	78.6	21.5	(*R*)
100	93	90.5	84.7	28.5	(*R*)
80	661	94.4	82.2	38.5	(*R*)

Reaction conditions: T = 100°C; solvent = 20 ml (toluene/ethanol = 1/1); substrate = 0.038 mmol; substrate/catalyst = 2000 mol/mol; $P(H_2)$ = 130 bar.
[a] Ethyl (*E*)-2-methyl-2-butenoate is also formed.
[b] Optical purity measured on samples of purified product using the $[\alpha]_{max}$ value reported in the Experimental part.

genations carried out in the presence of catalyst **2** (Table 2).

A comparison of the data in Tables 1 and 2 does not reveal remarkable differences between the two catalytic precursors under investigation; in fact the catalytic activity is similar, even if complex **2**, containing MOBIPH, is in all but one case slightly more active than complex **1** containing BINAP. By contrast, complex **1** affords higher values of optical purities.

The influence of temperature on the enantioselectivity of the reaction has been tested in the case of the hydrogenation of tiglic acid in the presence of $[Ru_4(\mu\text{-}H)_4(CO)_{10}\{(S)\text{-}(-)\text{-BINAP}\}]$ (Table 3). As expected, on going from 120°C to 80°C the reaction rate slows down, while the o.p. increases from 21.5% to 38.5%. Below 80°C the activity of the catalyst is highly depressed and the reaction rate close to zero.

In Table 4 are reported the data for the hydrogenation of (*E*)-2-methyl-2-butenoic acid with several ruthenium diphosphine clusters. The results obtained with catalysts **1** and **2** are there compared with the literature values.

From these data (entries 1–4) it appears that using catalysts of the type $[Ru_4(\mu\text{-}H)_4(CO)_{10}\{P\text{–}P\}]$ the more effective ligand is BINAP which furnishes the highest optical purity (28.5%). This value, obtained with the monosubstituted BINAP derivative having the chiral information only on one of the ruthenium centres of the cluster, is comparable (entry 5) with that achieved when using the cluster $[Ru_4(\mu\text{-}H)_4(CO)_8\{(-)\text{-DIOP}\}_2]$ in which each ruthenium centre is coordinated by a phosphorus atom, as demonstrated by X-ray structure [16]. Therefore it might be possible that a cluster containing two BINAP ligands, having a higher content and a more symmetrical distribution of the phosphorus centres, may enhance the induction of chiral information from the catalyst to the substrate leading to higher o.p. For such reasons, studies are in progress to synthesise BINAP or MOBIPH derivatives of general formula $[Ru_4(\mu\text{-}H)_4(CO)_8\{P\text{–}P\}_2]$.

3. Experimental

Solvents were purified by standard methods [17].

Table 4
Hydrogenation of tiglic acid in the presence of tetrahedral Ru clusters containing different chiral phosphine ligands

Catalyst	R [a] (mol/mol)	T (°C)	t (h)	Conversion [b] (%)	o.p. [c] (%)	Configuration	Solvent
$[Ru_4(\mu\text{-}H)_4(CO)_{10}\{(S)\text{-}(-)\text{-BINAP}\}]$	2000	100	93	90.5	28.5	(*R*)	toluene/ethanol (1/1)
$[Ru_4(\mu\text{-}H)_4(CO)_{10}\{(S)\text{-}(-)\text{-MOBIPH}\}]$	2000	100	72	100	16.7	(*S*)	toluene/ethanol (1/1)
$[Ru_4(\mu\text{-}H)_4(CO)_{10}\{(2S,3S)\text{-}(-)\text{-CHIRAPHOS}\}]$ [d]	1000	120	48	33.0	13.8	(*R*)	toluene
$[Ru_4(\mu\text{-}H)_4(CO)_{10}\{(S)\text{-}(-)\text{-BINAP}\}]$	1000	120	18	97.7	23.3	(*R*)	toluene
$[Ru_4(\mu\text{-}H)_4(CO)_8\{(2R,3R)\text{-}(-)\text{-DIOP}_2\}]$ [e]	325	100	20–40	80.0	31.0	(*S*)	toluene/ethanol (1/1)

Reaction conditions: T = 100°C; solvent = 20 ml; substrate = 0.038 mmol; $P(H_2)$ = 130 bar.
[a] Substrate/catalyst.
[b] Ethyl (*E*)-2-methyl-2-butenoate is also formed.
[c] Optical purity measured on samples of purified product using the $[\alpha]_{max}$ value reported in the Experimental part.
[d] Ref. [15].
[e] Ref. [13].

Table 5
The $[\alpha]_{D,max}$ values used to calculate the o.p. of the hydrogenation products

Product	$[\alpha]_{D,max}$ (at 25°C)	Configuration	Ref.
2-methylbutanoic acid	+19.8 (neat, d_{25} = 0.93)	(*S*)	[23]
ethyl 2-methylbutanoate	+17.8 (neat, d_{25} = 0.86)	(*S*)	[24]
1-phenylethanol	+43.6 (neat, d_{25} = 1.01)	(*R*)	[25]
2-phenyl-3,3-dimethylbutane	+25.7 (neat, d_{25} = 0.87)	(*S*)	[26]
2-methylsuccinic acid	+17.09 (*c* 4.42 in EtOH)	(*R*)	[27]
2-phenylpropanoic acid	−75.3 (*c* 1.6 in $CHCl_3$)	(*R*)	[28]

The atropoisomeric diphosphine ligands, (*S*)-(−)-BINAP [1] and (*S*)-(−)-MOBIPH [18], and the ruthenium cluster $[Ru_4(\mu\text{-}H)_4(CO)_{12}]$ [19] were synthesised as described in literature.

The diphosphine substituted clusters $[Ru_4(\mu\text{-}H)_4(CO)_{10}\{(S)\text{-}(-)\text{-BINAP}\}]$ and $[Ru_4(\mu\text{-}H)_4(CO)_{10}\{(S)\text{-}(-)\text{-MOBIPH}\}]$ have been synthesised and characterised (X-ray crystallographic data, ^1H and ^{31}P NMR data) as previously reported [12].

2-Phenyl-3,3-dimethyl-1-butene [20] and atropic acid [21,22] have been synthesised according to standard methods; all other substrates have been purchased from Aldrich. The $[\alpha]_{D,max}$ values used as references to calculate the o.p. of the hydrogenation products are listed in Table 5.

GLC and GLC–MS analyses were carried out on a Hewlett-Packard HP 5890 gas chromatograph interfaced to a HP 5971A quadrupole mass detector.

NMR spectra were carried out with a Bruker AC 200 spectrometer in $CDCl_3$ solution.

Optical rotations were carried out with a Perkin Elmer polarimeter model 241 using a cell with quartz windows of 1 dm length and 0.8 ml capacity.

The hydrogenation apparatus consists of a magnetically stirred 150 ml stainless steel autoclave equipped with valves, manometer and heating circuit.

In a typical experiment the substrate is introduced under N_2 in a 100 ml Schlenk tube together with dry and degassed solvent. After the addition of the catalyst, the resulting homogeneous reaction mixture is introduced via canula under N_2 into the autoclave. The reactor is then pressurised with H_2 and heated with a thermostatic bath (±0.1°C). After the desired reaction time the autoclave is cooled at room temperature, the residual gas removed and the reaction mixture analysed by GLC, GLC–MS and NMR spectroscopy.

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